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Editorial

Stiff-man syndrome

Stiff-man syndrome (SMS) is a rare neurological disorder first described by Moersch and Woltman in 1956.[1] The syndrome is of insidious onset, usually in the fourth or fifth decades, and affects both sexes equally.[2] Painful involuntary stiffness of the back due to continuous contraction of lumbar and abdominal muscles is the earliest symptom. Axial rigidity progresses slowly over months or years and is accompanied by spasms. Spontaneous spasmodic attacks occur in the majority of patients and are preceded by an aura-like feeling in some patients.[3] A stereotyped motor pattern is seen during these attacks, which consists of brief opisthotonos, stiffening of the slightly abducted legs and inversion of the plantar-fixed feet. Spasms are precipitated by voluntary movement, fright or sound and may be painful. A characteristic hyperlordosis of the lumbar spine is produced, due to contraction of thoracolumbar paraspinal muscles and abdominal wall rigidity.[4] Proximal limb muscles are affected later, but face and distal limbs are generally spared. The axial and proximal limb muscle rigidity is aggravated by sensory stimuli and abolished by sleep and anaesthesia.[1] As the disease progresses, the voluntary movements of the trunk and legs become slow and restricted.

The pathophysiology of SMS is ill understood. It may be an autoimmune disease, based on its frequent association with a number of autoimmune diseases and the findings of a variety of autoantibodies. Insulin-dependent diabetes mellitus (IDDM) is present in one- to two-thirds of patients.[5,6] Autoimmune thyroid disease, pernicious anaemia, vitiligo, myasthenia gravis, thymoma, alopecia totalis and certain malignancies are more common in SMS patients, while epilepsy occurs in 10% of patients.[7]

Autoantibodies against gamma-aminobutyric acid (GABA)-ergic neurons have been detected in serum and cerebrospinal fluid in 60% of patients with a clinical diagnosis of SMS.[6] In one series,[8] thyrogastric antibodies were more frequent in patients with SMS (46%) than in those with other neurological disorders (12%). Islet-cell antibodies and anti-glutamic acid decarboxylase (anti-GAD) antibodies were more common in the SMS patients (38% and 31%, respectively) than in the patients with other neurological disorders (6% and 3%, respectively). Four of the 13 patients with SMS had an associated solid tumour and three had antibodies to 125/130 kd protein (paraneoplastic variant). Autoantibodies against amphiphysin (a protein associated with synaptic vesicles and expressed in many neurons, certain endocrine cell types and spermatocytes) have been described in patients with paraneoplastic SMS.[9,10]

Clinical features of SMS

- painful involuntary stiffness of the back is the earliest symptom
- spontaneous spasmodic attacks occur in a majority of patients
- spasms are precipitated by voluntary movement, fright or sound
- hyperlordosis of the lumbar spine is produced due to contraction of thoracolumbar paraspinal muscles and abdominal wall rigidity
- the axial and proximal limb muscle rigidity is aggravated by sensory stimuli and abolished by sleep and anaesthesia
- in late stages, the voluntary movements of the trunk and legs become slow and restricted

Box 1

Diseases associated with SMS

- IDDM
- autoimmune thyroid disease
- pernicious anaemia
- vitiligo
- myasthenia gravis
- thymoma
- alopecia totalis
- malignancy
- epilepsy

Box 2

Autoantibodies found in SMS

- against GABA-ergic neurons
- thyrogastric antibodies
- islet-cell antibodies
- anti-GAD antibodies
- antibodies to 125/130 kd protein
- autoantibodies against amphiphysin

Box 3

Electromyography of affected muscles reveals nonspecific findings and demonstrates involuntary motor unit activity. The appearance and firing pattern of motor units are normal except that agonist and antagonist muscles may contract concurrently.[11] Peripheral nerve conduction is normal. Oligoclonal IgG bands have been reported in several cases.[12–14] Association with HLA B44[15,16] antigen and DR3[14] and 4 antigens have been reported.

An imbalance between descending aminergic effects and the inhibitory effects of GABA in the brainstem and the spinal cord has been suggested as a cause of abnormal excitability of spinal interneuronal networks.[8,17–22] This hypothesis is supported by the observations that the drugs that increase aminergic (noradrenergic or serotonergic) activity in the central nervous system such as levodopa,[20] clomipramine,[17] reserpine[17] and metamphetamine,[18] increase the severity of spasms, while those that reduce central catecholamine effects, such as clonidine[17,18] and tizanidine,[18] or enhance GABA activity (baclofen or benzodiazepines), diminish the spasms.

Benzodiazepines and baclofen help reduce spasms. Other drugs used with reported benefit are sodium valproate, tizanidine, vigabatrin,[23] and botulinum toxin A.[24] Favourable responses to plasmapheresis[25] and intravenous immunoglobulin therapy[26] have also been reported. Plasmapheresis has been used alone and in conjunction with steroids.

In conclusion, research findings support the theory of central nervous system autoimmunity with resultant impairment of neuronal pathways as the probable pathogenesis of stiff-man syndrome.

SMS is a heterogenous disorder and can be divided into three main types:

- patients (mostly female) with associated autoimmune diseases (mainly IDDM), who are positive for islet-cell antibodies and anti-GAD antibodies but negative for non-organ-specific autoantibodies (autoimmune SMS).
- patients (mostly male) with associated neoplasms and non-organ-specific autoantibodies who are negative for islet-cell autoantibodies; SMS patients with no other associated clinical condition but with high GAD antibodies or organ-specific autoantibodies (paraneoplastic SMS)
- patients with no other associated clinical condition but a high prevalence of non-organ-specific autoantibodies, anti-GAD antibodies, or organ-specific antibodies (idiopathic SMS).

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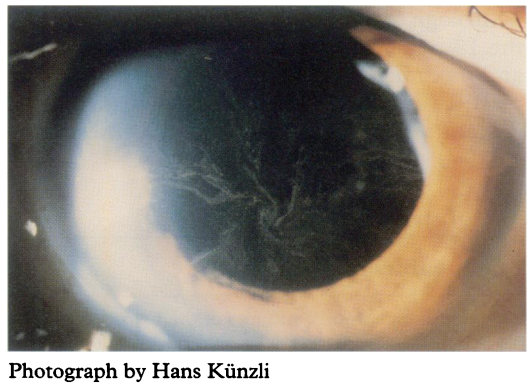
Images in medicine

Amiodarone-induced cornea verticillata

A 71-year-old man was treated for recurrent ventricular tachycardia with 200 mg amiodarone daily for 15 months. During therapy, golden-grey deposits appeared in a vortex fashion in the corneal epithelium of both eyes just below the central cornea. His visual acuity had also decreased during the last 2 years from 20/20 to 20/30, accompanied by an altered colour perception, glare and blurring. He was referred to our clinic to see whether these changes could be attributed to the corneal deposits. Examination revealed opacity of both lenses and the described corneal findings. A diagnosis of bilateral senile cataract and cornea verticillita was made. After removal of the cataracts, visual acuity improved and visual symptoms disappeared; the corneal changes have remained stable under amiodarone therapy for the last 2 years (figure).

Corneal deposits may be observed in 70–100% of patients under amiodarone treatment but do not usually threaten vision or need routine ophthalmologic surveillance.



Photograph by Hans Künzli

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